WE CLAIM

1. A compound of Formula I:

in which:

n is chosen from 0, 1 and 2; m is chosen from 1, 2 and 3;

 R_1 is chosen from $C_{6\text{-}10}$ aryl and $C_{5\text{-}10}$ heteroaryl; wherein any aryl or heteroaryl of R_1 is optionally substituted by a radical chosen from $C_{6\text{-}10}$ aryl $C_{0\text{-}4}$ alkyl, $C_{5\text{-}6}$ heteroaryl $C_{0\text{-}4}$ alkyl, $C_{3\text{-}8}$ cycloalkyl $C_{0\text{-}4}$ alkyl, $C_{3\text{-}8}$ heterocycloalkyl $C_{0\text{-}4}$ alkyl or $C_{1\text{-}10}$ alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by 1 to 5 radicals chosen from halo, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo-substituted- $C_{1\text{-}10}$ alkyl and halo-substituted- $C_{1\text{-}10}$ alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from -S-, -S(O)-, -S(O)2-, $-NR_7$ - and -O-; wherein R_7 is chosen from hydrogen and $C_{1\text{-}6}$ alkyl;

 R_2 , R_3 , R_4 and R_5 are independently chosen from hydrogen, halo, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy;

A is chosen from $-X_1C(O)OR_7$, $-X_1OP(O)(OR_7)_2$, $-X_1P(O)(OR_7)_2$, $-X_1P(O)(OR_7)_2$, $-X_1P(O)OR_7$, $-X_1P(O)OR_7$, $-X_1P(O)OR_7$, and 1*H*-tetrazol-5-yl; wherein X_1 is chosen from a bond, C_{1-3} alkylene and C_{2-3} alkenylene and R_7 is chosen from hydrogen and C_{1-6} alkyl;

B is CR_8R_9 ; wherein R_8 and R_9 are independently chosen from hydrogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy;

E is chosen from CR_8 or N; wherein R_8 is chosen from hydrogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy; or B is CR_9 and E is carbon and B and E are connected via a double bond;

X is a bond or is chosen from $-X_1OX_2-$, $-X_1NR_7X_2-$, $-X_1C(O)NR_7X_2-$, $-X_1NR_7C(O)X_2-$, $-X_1S(O)X_2-$, $-X_1S(O)_2X_2-$, $-X_1SX_2-$, C_{4-6} heteroarylene and $-X_1ON=C(R_7)X_2-$; wherein X_1 and X_2 are independently chosen from a bond, C_{1-3} alkylene and C_{2-3} alkenylene; R_7 is chosen from hydrogen and C_{1-6} alkyl; and any heteroarylene of X is optionally substituted by a member of the group chosen from halo and C_{1-6} alkyl;

- Y is chosen from C_{6-10} aryl and C_{5-10} heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydoxy, nitro, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted C_{1-10} alkyl and halo-substituted C_{1-10} alkoxy; and the pharmaceutically acceptable salts, hydrates, solvates, isomers and prodrugs thereof.
- 2. The compound of claim 1 in which R_1 is chosen from phenyl, naphthyl and thiophenyl optionally substituted by C_{6-10} aryl C_{0-4} alkyl, C_{5-6} heteroaryl C_{0-4} alkyl, C_{3-8} heterocycloalkyl C_{0-4} alkyl or C_{1-10} alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by 1 to 5 radicals chosen from halo, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from -S-, -S(O)-, $-S(O)_2-$, $-NR_7-$ and -O-; wherein R_7 is hydrogen or C_{1-6} alkyl.
- 3. The compound of claim 1 in which A is chosen from $-X_1C(O)OR_7$ and 1*H*-tetrazol-5-yl; wherein X_1 is chosen from a bond, C_{1-3} alkylene and C_{2-3} alkenylene and R_7 is chosen from hydrogen and C_{1-6} alkyl.
 - 4. The compound of claim 1 in which X is chosen from:

wherein the left and right asterisks of X indicate the point of attachment between R_1 and Y of Formula I, respectively; R_7 is chosen from hydrogen and C_{1-6} alkyl; v and w are independently 0, 1, 2 or 3.

5. The compound of claim 1 in which Y is chosen from:

wherein R_7 is hydrogen or $C_{1\text{-}6}$ alkyl; and the left and right asterisks of Y indicate the point of attachment between X and E of Formula I, respectively.

6. The compound of claim 2 in which R_1 is chosen from:

$$R_{10}$$
 and R_{11} R_{10} R_{10} R_{10}

wherein the asterisk is the point of attachment of R_1 with X; R_{10} is $C_{6\text{-}10}$ aryl $C_{0\text{-}4}$ alkyl, $C_{5\text{-}6}$ heteroaryl $C_{0\text{-}4}$ alkyl, $C_{3\text{-}8}$ cycloalkyl $C_{0\text{-}4}$ alkyl, $C_{3\text{-}8}$ heterocycloalkyl $C_{0\text{-}4}$ alkyl or $C_{1\text{-}10}$ alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_{10} can be optionally substituted by 1 to 3 radicals chosen from halo, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halosubstituted- $C_{1\text{-}10}$ alkyl and halo-substituted- $C_{1\text{-}10}$ alkoxy; and any alkyl group of R_{10} can optionally have a methylene replaced by an atom or group chosen from $-S_{-}$, $-S(O)_{-}$, $-S(O)_{2-}$, $-NR_{7-}$ and $-O_{-}$; wherein R_{7} is hydrogen or $C_{1\text{-}6}$ alkyl; and R_{11} is selected from halo, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo-substituted- $C_{1\text{-}10}$ alkyl and halo-substituted- $C_{1\text{-}10}$ alkoxy.

7. The compound of claim 2 selected from: 3-{4-[6-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyridin-3-yl]-piperazin-1-yl}-propionic acid; 3-{4-[6-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyridin-3-yl]-piperazin-1-yl}-piper

Cyclohexyl-3-trifluoromethyl-phenoxymethyl)-pyridin-3-yl]-piperazin-1-yl}-propionic acid; 3-{4-[6-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyridazin-3-yl]-piperazin-1-yl}propionic acid; 3-{4-[2-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-pyrimidin-5-yl]piperazin-1-yl}-propionic acid; 3-{4-Hydroxy-4-[2-(2-trifluoromethyl-biphenyl-4-yl)benzo[b]thiophen-5-yl]-piperidin-1-yl}-propionic acid; 3-{4-[2-(2-Trifluoromethylbiphenyl-4-yl)-benzo[b]thiophen-5-yl]-3,6-dihydro-2H-pyridin-1-yl}-propionic acid; 3-(3-{4-[3-(2-Trifluoromethyl-biphenyl-4-yl)-[1,2,4]oxadiazol-5-yl]-phenyl}-pyrrolidin-1-yl)propionic acid; 3-(3-{3-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{3-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{4-[3-(4-Cyclohexyl-3trifluoromethyl-phenyl)-[1,2,4]oxadiazol-5-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(4-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-(3-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(3-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-pyrrolidin-1-yl)-propionic acid; 3-(4-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-(3-{4-[5-(4-Cyclohexyl-3-trifluoromethyl-phenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}azetidin-1-yl)-propionic acid; 3-(3-{4-[5-(2-Trifluoromethyl-biphenyl-4-yl)-[1,3,4]oxadiazol-2-yl]-phenyl}-azetidin-1-yl)-propionic acid; 3-(4-{4-[5-(3-Trifluoromethylphenyl)-[1,3,4]oxadiazol-2-yl]-phenyl}-piperidin-1-yl)-propionic acid; 3-{4-[6-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-pyridin-3-yl]-piperazin-1-yl}-propionic acid; and 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-ylsulfanylmethyl)-phenyl]-piperidin-1-yl}-propionic acid.

8. The compound of claim 2 of Formula Ia:

HO
$$N \stackrel{\text{Ho}}{\underset{\text{R}_{12}}{\bigvee}} \mathbb{R}_{10}$$

$$(Ia)$$

in which:

E is selected from N and CH;

m and n are independently selected from 0 and 1;

v and w are independently selected from 0 and 1;

 R_{10} is selected from cyclohexyl, piperidinyl, tetrahydro-thiopyran-4-yl, phenyl, phenoxy and phenylsulfanyl; wherein any cyclohexyl, piperidinyl, tetrahydro-thiopyran-4-yl, phenyl, phenoxy and phenylsulfanyl of R_{10} can be optionally substituted by 1 to 3 radicals independently selected from methyl and isopropyl;

R₁₁ is selected from methyl, trifluoromethyl and ethyl; and

R₁₂ is selected from hydrogen, ethyl and methoxy.

9. The compound of claim 8 selected from: 3-{4-[4-(4-Cyclohexyl-3-methylphenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Piperidin-1-yl-3trifluoromethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-(4-{4-[3-Methyl-4-(tetrahydro-thiopyran-4-yl)-phenoxymethyl]-phenyl}-piperidin-1-yl)-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-piperidin-1-yl}-propionic acid; 3- $\{4-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-2-ethyl-phenyl]-piperazin-1-yl\}-1-yl-pheny$ propionic acid; 3-{4-[4-(2-Methyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}propionic acid; 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxymethyl)-phenyl]piperidin-1-yl}-propionic acid; 3-{4-[4-(3'-Methyl-2-trifluoromethyl-biphenyl-4yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{3-[4-(4-Cyclohexyl-3trifluoromethyl-phenoxymethyl)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-ethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-pyrrolidin-1-yl}-propionic acid; 3-(4-{4-[4-(3,6-Dihydro-2H-thiopyran-4-yl)-3-trifluoromethyl-phenoxymethyl]-phenyl}-piperidin-lyl)-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)-phenyl]-azetidin-1yl}-propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-azetidin-1yl}-propionic acid; 3-{4-[2-Ethyl-4-(2-trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]piperidin-1-yl}-propionic acid; 3-{3-[4-(4-Cyclohexyl-3-trifluoromethyl-benzyloxy)phenyl]-pyrrolidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-

benzyloxy)-2-ethyl-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4'-Methyl-2trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Phenoxy-3-trifluoromethyl-phenoxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(4-Cyclohexyl-3-trifluoromethyl-phenoxymethyl)-2-methoxy-phenyl]-piperazin-1-yl}propionic acid; 3-{4-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidin-1-yl}propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-pyrrolidin-1-yl}propionic acid; 3-{3-[4-(2-Trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-azetidin-1-yl}propionic acid; 3-{4-[4-(4-Isobutyl-3-trifluoromethyl-benzyloxy)-phenyl]-piperidin-1-yl}propionic acid; 3-{4-[4-(4-Phenylsulfanyl-3-trifluoromethyl-phenoxymethyl)-phenyl]piperidin-1-yl}-propionic acid; 1-(1H-Tetrazol-5-ylmethyl)-4-[4-(2-trifluoromethylbiphenyl-4-ylmethoxy)-phenyl]-piperidine; 1-[2-(1H-Tetrazol-5-yl)-ethyl]-4-[4-(2trifluoromethyl-biphenyl-4-ylmethoxy)-phenyl]-piperidine; 3-{4-[4-(2,4'-Dimethylbiphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2,4'-Dimethylbiphenyl-4-ylmethoxy)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Ethyl-biphenyl-4vloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; 3-{4-[4-(2-Ethyl-3'-methyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-propionic acid; (2-{4-[4-(2-Trifluoromethylbiphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-ethyl)-phosphonic acid; 2-{4-[4-(2-Trifluoromethyl-biphenyl-4-yloxymethyl)-phenyl]-piperidin-1-yl}-ethanesulfonic acid; and Phosphoric acid mono-(2-{4-[4-(2-trifluoromethyl-biphenyl-4-yloxymethyl)-phenyllpiperidin-1-yl}-ethyl) ester.

- 10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a pharmaceutically acceptable excipient.
- 11. A method for treating a disease in an animal in which alteration of EDG/S1P receptor mediated signal transduction can prevent, inhibit or ameliorate the pathology and/or symptomology of the disease, which method comprises administering to the animal a therapeutically effective amount of a compound of Claim 1.
- 12. A method for preventing or treating disorders or diseases mediated by lymphocytes, for preventing or treating acute or chronic transplant rejection or T-cell

mediated inflammatory or autoimmune diseases, for inhibiting or controlling deregulated angiogenesis, or for preventing or treating diseases mediated by a neo-angiogenesis process or associated with deregulated angiogenesis in a subject comprising administering to the subject in need thereof an effective amount of a compound of claims I, or a pharmaceutically acceptable salt thereof.

- 13. The use of a compound of claim 1 in the manufacture of a medicament for treating a disease in an animal in which alteration of EDG/S1P receptor mediated signal transduction contributes to the pathology and/or symptomology of the disease.
 - 14. A process for preparing a compound of Formula I:

in which:

n is chosen from 0, 1 and 2; m is chosen from 1, 2 and 3;

 R_1 is chosen from $C_{6\text{-}10}$ aryl and $C_{5\text{-}10}$ heteroaryl; wherein any aryl or heteroaryl of R_1 is optionally substituted by a radical chosen from $C_{6\text{-}10}$ aryl $C_{0\text{-}4}$ alkyl, $C_{5\text{-}6}$ heteroaryl $C_{0\text{-}4}$ alkyl, $C_{3\text{-}8}$ ecycloalkyl $C_{0\text{-}4}$ alkyl, $C_{3\text{-}8}$ heterocycloalkyl $C_{0\text{-}4}$ alkyl or $C_{1\text{-}10}$ alkyl; wherein any aryl, heteroaryl, cycloalkyl or heterocycloalkyl group of R_1 can be optionally substituted by 1 to 5 radicals chosen from halo, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo-substituted- $C_{1\text{-}10}$ alkyl and halo-substituted- $C_{1\text{-}10}$ alkoxy; and any alkyl group of R_1 can optionally have a methylene replaced by an atom or group chosen from -S-, -S(O)-, -S(O)2-, $-NR_7$ - and -O-; wherein R_7 is chosen from hydrogen and $C_{1\text{-}6}$ alkyl;

 R_2 , R_3 , R_4 and R_5 are independently chosen from hydrogen, halo, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy;

A is chosen from $-X_1C(O)OR_7$, $-X_1OP(O)(OR_7)_2$, $-X_1P(O)(OR_7)_2$, $-X_1P(O)OR_7$, $-X_1S(O)_2OR_7$, $-X_1P(O)(R_7)OR_7$ and 1H-tetrazol-5-yl; wherein X_1 is chosen from a bond, C_{1-3} alkylene and C_{2-3} alkenylene and R_7 is chosen from hydrogen and C_{1-6} alkyl;

B is CR_8R_9 ; wherein R_8 and R_9 are independently chosen from hydrogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy;

E is chosen from CR_8 or N; wherein R_8 is chosen from hydrogen, hydroxy, C_{1-10} alkyl, C_{1-10} alkoxy, halo-substituted- C_{1-10} alkyl and halo-substituted- C_{1-10} alkoxy; or B is CR_9 and E is carbon and B and E are connected via a double bond;

is a bond or is chosen from $-X_1OX_2$ -, $-X_1NR_7X_2$ -, $-X_1C(O)NR_7X_2$ -, $-X_1NR_7C(O)X_2$ -, $-X_1S(O)X_2$ -, $-X_1S(O)_2X_2$ -, $-X_1SX_2$ -, C_{4-6} heteroarylene and $-X_1ON$ = $C(R_7)X_2$ -; wherein X_1 and X_2 are independently chosen from a bond, C_{1-3} alkylene and C_{2-3} alkenylene; R_7 is chosen from hydrogen and C_{1-6} alkyl; and any heteroarylene of X is optionally substituted by a member of the group chosen from halo and C_{1-6} alkyl;

Y is chosen from $C_{6\text{-}10}$ aryl and $C_{5\text{-}10}$ heteroaryl, wherein any aryl or heteroaryl of Y can be optionally substituted with 1 to 3 radicals chosen from halo, hydoxy, nitro, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, halo-substituted $C_{1\text{-}10}$ alkyl and halo-substituted $C_{1\text{-}10}$ alkoxy; which process comprises:

(a) reacting a compound of formula 2:

Boc
$$R_3$$
 R_2 R_5 R_4 R_5 R_5 R_4 R_5 R_4 R_5 R_5 R_4 R_5 R_5

with either t-butyl acrylate, acylonitrile/NaN₃ or bromoacetonitrile/NaN₃; wherein B, E, Y, X, R₁ R₂, R₃, R₄ and R₅ are as described above; and

- (b) optionally converting a compound of the invention into a pharmaceutically acceptable salt;
- (c) optionally converting a salt form of a compound of the invention to a non-salt form;
- (d) optionally converting an unoxidized form of a compound of the invention into a pharmaceutically acceptable N-oxide;
- (e) optionally converting an N-oxide form of a compound of the invention to its unoxidized form;

(f) optionally resolving an individual isomer of a compound of the invention from a mixture of isomers;

- (g) optionally converting a non-derivatized compound of the invention into a pharmaceutically acceptable prodrug derivative; and
- (h) optionally converting a prodrug derivative of a compound of the invention to its non-derivatized form.